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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/486,839	03/01/2000	RAJA G. ACHARI	719-75-PCT/U	4232

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EXAMINER

JIANG, SHAOJIA A

ART UNIT	PAPER NUMBER
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1617

DATE MAILED: 02/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/486,839	ACHARI ET AL.	
	Examiner	Art Unit	
	Shaojia A Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 September 2003 and 20 October 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 23-26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 23-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This Office Action is a response to Applicant's amendment and response filed on September 9, 2003 and October 20, 2003 wherein claims 1-22 are cancelled and claims 23-26 are newly submitted. Currently, claims 23-26 are pending in this application.

Claims 23-26 are examined on the merits herein.

The following is new rejections.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-26 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for treating nausea and/or vomiting and/or motion sickness in a mammal disclosed in the specification employing the instant formulation herein, does not reasonably provide enablement for the **preventing** nausea and/or vomiting and/or motion sickness by administering such a composition to a mammal in need thereof.

The instant claims are drawn to the method for the **preventing** nausea and/or vomiting and/or motion sickness. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed

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to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApl's 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: The instant invention pertains to the method of **preventing** nausea and/or vomiting and/or motion sickness in a mammal.

The state of the prior art: The skilled artisan would view that the treatment to prevent nausea and/or vomiting and/or motion sickness in a mammal in a human or a mammal totally, absolutely, or permanently, is highly unlikely, not even occurring at the first time.

The relative skill of those in the art: The relative skill of those in the art is high.

The predictability or lack thereof in the art: The skilled artisan would view that the treatment to prevent nausea and/or vomiting and/or motion sickness in a mammal in a human or a mammal totally, absolutely, or permanently is highly unpredictable, and not even occur at the first time is highly unpredictable.

The amount of direction or guidance presented and the presence or absence of working examples: In the instant case, **no** working examples are presented in the specification as filed showing how to prevent nausea and/or vomiting and/or motion

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sickness in a mammal in a human or a mammal totally, absolutely, or permanently, not even occurring at the first time.

Genentech, 108 F.3d at 1366, states that “a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion” and “[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable”.

Therefore, in view of the Wands factors, as discussed above, e.g., the amount of direction or guidance provided, absence of working examples, and the predictability of the art, Applicants fail to provide information sufficient to practice the claimed invention.

Applicant is suggested to amend these claims by deleting “preventing”.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 23-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation “20 mM” in claim 23 is unclear as to whose concentration would be, i.e., whether the concentration of scolpolamine hydrobromide which is also considered a salt to one of ordinary skill in the art, or polyvinyl alcohol or the buffer salt concentration. The specification disclosing:

“Nasal gel Formulation 2 containing PVA gelling agent at a pl-I of about 3.5 and

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having a scopolamine concentration of about 0.2 mg/0.1 gm at a buffer concentration of 0.02M (20 mM) was prepared as follows" (see page 12 the last paragraph).

One of ordinary skill in the art would recognize that the amount 0.2 mg would not necessarily be 20 mM.

The recitation "administering a scopolamine hydrobromide formulation to a mammal in need thereof" in claim 25 is missing. Applicant is suggested to amend these claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 23-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keith (WO 83/00286, of record) in view of JOSHI et al. (5,252,318, of record) and *Handbook of Pharmaceutical Excipients*, 2nd Ed, page 383 (provided by Applicant in the response in Paper No. 14).

Keith discloses that an intranasal formulation comprising scopolamine hydrochloride in a pharmaceutically acceptable carrier, an aqueous solution containing ethanol, an aerosol spray vehicle, is useful in a method of preventing and/or treating

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motion sickness such as nausea and/or vomiting. See abstract, Examples I-XII, and claims 1-6. Keith also discloses that the intranasal formulation therein provides quick relief from motion sickness and the onset of effect is within ten minutes. See page 2 lines 3-4, page 3 Example II, and page 4 Example IV.

The prior art does not expressly disclose that the pH value of the instant intranasal formulation is about 3.5, and the concentration of the buffer salt in the instant intranasal formulation is about 20 mM. The prior art does also not expressly disclose the employment of polyvinyl alcohol in the formulation in combination with one or more additional gelling agents or bioadhesives such as alginates, gums, and starches in the instant intranasal formulation and method for the treatment of motion sickness.

Handbook of Pharmaceutical Excipients teaches polyvinyl alcohol is a known viscosity increasing agent (also known as a thickening agent) and a known lubricant (page 383).

Joshi et al. discloses that drug delivery systems such as gelling aqueous compositions therein undergo significant changes in viscosity in response to substantially changes in pH and temperature (see abstract). Joshi et al. also teaches that by adjusting or controlling the pH of these drug delivery systems in an aqueous base through the addition of buffering agents, the viscosities of the compositions or formulations may be various (see col.1 lines 6-15, and col.2 lines 1-5 and 21-28). Joshi et al. also discloses that compositions or formulations therein exhibit steady state flow characteristics at or near room temperature at a pH range of 2.5 to 6.5, i.e., a pH of between 3.0 and 5.0 (see col.3 lines 33-35, and col.7-8 especially lines 57-59). Joshi et

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al. discloses the employment of lubricants such as polyvinyl alcohol (see col.12 lines 21-22) in combination with one or more additional gelling agents or bioadhesives in the formulations (see col.3 lines 24-48). Joshi et al. further discloses that the most promising drugs for incorporating into the aqueous drug delivery compositions therein include scopolamine (see col.11 lines 32-33).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to optimize the pH of the intranasal formulation herein to about 3.5 and the concentration of the buffer salt in the instant intranasal formulation to below about 20 mM, to employ polyvinyl alcohol in combination with one or more additional gelling agents or bioadhesives in the instant intranasal formulation and method for the treatment of nausea and/or vomiting associated with motion sickness.

One having ordinary skill in the art at the time the invention was made would have been motivated to optimize the pH of the instant intranasal formulation to about 3.5 and the concentration of the buffer salt in the instant intranasal formulation to about 20 mM, since gelling aqueous compositions in drug delivery systems are known to significantly change in viscosity in response to changes in pH and temperature according to Joshi et al. Joshi et al. also teaches that by adjusting or controlling the pH of these drug delivery systems in an aqueous base through the addition of buffering agents, the viscosities of the compositions or formulations may be various. Gelling aqueous compositions or formulations therein are known to exhibit steady state flow characteristics at or near room temperature at a pH range of 2.5 to 6.5, i.e., a pH of between 3.0 and 5.0 according to Joshi et al. Scopolamine is known to be one of the

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most promising drugs for incorporating into the aqueous drug delivery compositions of Joshi et al.

Therefore, one of ordinary skill in the art would find it obvious to optimize the pH by adjusting the concentration of buffering agents in order to make the formulations herein having optimized viscosities exhibiting steady state flow characteristics at or near room temperature since the optimization of parameters based on the known information, i.e., known pH range of 2.5 to 6.5, is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art. It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980). Thus, Joshi et al. clearly provided the motivation and knowledge to optimize the pH and concentration of the buffering agents in the drug delivery system for scopolamine.

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Applicant's remarks filed on September 9, 2003 with respect to the rejection of claims 1-21 made under 35 U.S.C. 103(a) as being unpatentable over Keith in view of Osol et al. for reasons of record stated in the Office Action dated April 9, 2009 have been fully considered but are moot in view of the new ground(s) of rejection set forth above.

Additionally, Applicant's assertion that Formulation 2 of the specification demonstrates unexpected superior property has been considered. However, the clear

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explanation of pointing out exactly what facts are established therein and relied upon by applicant is not seen in the specification (see page 20). Applicant has the burden to explain the experimental evidence. See *In re Borkowski and Van Venrooy* 184 USPQ 29 (CCPA 1974).

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-

1235.



S. Anna Jiang, Ph.D.
Patent Examiner, AU 1617
February 11, 2004